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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/737,270 | 12/16/2003 | William D. Thomas JR. | 06132/045004 | 6163 |

21559 7590 10/20/2004

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| EXAMINER | |
|---|---|
| TONGUE, LAKIA J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/737,270 | THOMAS ET AL. | |
| | Examiner | Art Unit | |
| | Lakia J Tongue | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) 1-11 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 12-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

***Election/Restrictions***

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11, drawn to a method of treating *C. difficile* infection comprising administering *Clostridium difficile* toxin-neutralizing polyclonal immune globulin to a human, classified in class 424, subclass 167.1.

II. Claims 12-17, drawn to a method of preventing or treating *C. difficile* comprising administering a toxin or toxoid to a human patient, classified in class 424, subclass 236.1, 239.1 and 247.1. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are methods of treating using different reagents. Group I is a method of treating *C. difficile* infection by administering antibodies. Group II is a method of treating *C. difficile* infection by administering antigens.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Susan Michaud on July 12, 2004 a provisional election was made without traverse to prosecute the invention of Group II,

claims 12-17. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-11 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

## DETAILED ACTION

### *Priority*

1. Applicant is receiving the December 16, 2003 filing date of the instant application because the priority document does not show the administration of *Clostridium* toxin to a patient.

### *Information Disclosure Statement*

2. The information disclosure statement filed January 26, 2004 has been considered. The items crossed off are not under consideration. The crossed off documents were not found in either the CIP (09/815,452) or the provisional (60/062,522).

### *Claim Rejections - 35 USC § 102*

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 12-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kotloff et al., ("Safety and Immunogenicity of Increasing Doses of a *Clostridium difficile* Toxoid

Vaccine Administered to Healthy Adults", Infection and Immunity, (2001 Feb.) 69(2) 988-98).

Claims 12-17 are drawn to a method of preventing or treating symptomatic *Clostridium difficile* infection by administering percutaneously a clostridial toxin or toxoid to a human.

Kotloff et al discloses an effective vaccine containing *C. difficile* toxoids A and B that can be used to elicit protective immunity in individuals at high risk for *C. difficile*-associated diarrhea (CDAD) (page 988). Kotloff et al discloses considerable evidence that supports the role of antibody-mediated anti-toxic immunity in protection and recovery from *C. difficile*-associated disease. Additionally, Kotloff et al discloses that in animal models of *C. difficile* infection, parenteral and mucosal administration of specific toxin-neutralizing monoclonal and polyclonal antibodies prevents experimentally induced *C. difficile*-associated enterotoxity (page 993). Lastly, Kotloff et al discloses the feasibility of preventing primary or relapsing CDAD by administering the vaccine to patients upon admission to the hospital or after an episode of CDAD (page 991-992).

***Conclusion***

4. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Williams (U.S. Patent 5,919,665) discloses an invention that contemplates vaccinating humans with anti-botulinal toxin, which is an antitoxin useful for the treatment of patients affected or at risk of symptoms due to the action of *C. botulinum*

toxins. A preferred embodiment of the method of the invention is directed toward obtaining antibodies against Clostridium species, their toxins, enzymes or other metabolic by-products, cell wall components, or synthetic or recombinant versions of any of those compounds. Examples of the toxins include toxins A and B of *C. difficile*. The route of immunization can be intramuscular or subcutaneously in addition to others.

B) Gerding (WO/97/09886) discloses an invention that provides methods and compositions for preventing and treating *Clostridium difficile*-associated disease in a human subject. A composition of a selected non-toxigenic strain of *C. difficile* is administered to a subject at risk.

C) Torres et al (Evaluation of Formalin-Inactivated *Clostridium difficile* Vaccines Administered by Parenteral and Mucosal Routes of Immunization in Hamsters, Infection and Immunity, Dec. 1995, p 4619-4627) discloses results that indicated optimal protection against *C. difficile* disease with combined parenteral and mucosal immunization.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakia J Tongue whose telephone number is 571-272-2921. The examiner can normally be reached on Monday-Friday 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ljt

L. R. F. Smith

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